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<!--StartFragment-->RESULT 1
US-08-690-102A-4
; Sequence 4, Application US/08690102A
; Patent No. 5789554
; GENERAL INFORMATION:
; APPLICANT: LEUNG, Shui-on
; APPLICANT: HANSEN, Hans
; TITLE OF INVENTION: IMMUNOCONJUGATES AND HUMANIZED
; TITLE OF INVENTION: ANTIBODIES SPECIFIC FOR B-CELL LYMPHOMA AND LEUKEMIA CELLS
; NUMBER OF SEQUENCES: 21
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Foley & Lardner
; STREET: 3000 K Street, N.W., Suite 500
; CITY: Washington, D.C.
; COUNTRY: USA
; ZIP: 20007-5109
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/690,102A
; FILING DATE: 01-JUL-1996
; CLASSIFICATION: 424
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 08/289,576
; FILING DATE: 12-AUG-1994
; ATTORNEY/AGENT INFORMATION:
; NAME: SAXE, Bernhard D.
; REGISTRATION NUMBER: 28,665
; REFERENCE/DOCKET NUMBER: 18733/463/IMIN
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (202)672-5300
; TELEFAX: (202)672-5399
; TELEX: 904136
; INFORMATION FOR SEQ ID NO: 4:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 116 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-690-102A-4

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Query Match          100.0%; Score 620; DB 1; Length 116;
Best Local Similarity 100.0%;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 QVQLQESGAELSKPGASVKMSCKASGYTFTSYWLHWIKQRPQGGLWIGYINPRNDYTEY 60
        |||
Db      1 QVQLQESGAELSKPGASVKMSCKASGYTFTSYWLHWIKQRPQGGLWIGYINPRNDYTEY 60

Qy      61 NQNFKDKATLTADKSSSTAYMQLSSLTSEDSAVYYCARRDITTFYWGQGTTLTVSS 116
        |||
Db      61 NQNFKDKATLTADKSSSTAYMQLSSLTSEDSAVYYCARRDITTFYWGQGTTLTVSS 116

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<!--EndFragment-->

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<!--StartFragment-->RESULT 1
US-08-690-102A-2
; Sequence 2, Application US/08690102A
; Patent No. 5789554
; GENERAL INFORMATION:
; APPLICANT: LEUNG, Shui-on
; APPLICANT: HANSEN, Hans
; TITLE OF INVENTION: IMMUNOCONJUGATES AND HUMANIZED
; TITLE OF INVENTION: ANTIBODIES SPECIFIC FOR B-CELL LYMPHOMA AND LEUKEMIA CELLS
; NUMBER OF SEQUENCES: 21
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Foley & Lardner
; STREET: 3000 K Street, N.W., Suite 500
; CITY: Washington, D.C.
; COUNTRY: USA
; ZIP: 20007-5109
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/690,102A
; FILING DATE: 01-JUL-1996
; CLASSIFICATION: 424
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 08/289,576
; FILING DATE: 12-AUG-1994
; ATTORNEY/AGENT INFORMATION:
; NAME: SAXE, Bernhard D.
; REGISTRATION NUMBER: 28,665
; REFERENCE/DOCKET NUMBER: 18733/463/IMIN
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (202)672-5300
; TELEFAX: (202)672-5399
; TELEX: 904136
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 113 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-690-102A-2

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Query Match          100.0%; Score 589; DB 1; Length 113;
Best Local Similarity 100.0%;
Matches 112; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 DIQLTQSPSSLAVSAGENVMTSCKSSQSVLYSANHKNYLAWYQQKPGQSPKLLIYWASTR 60
          |||
Db      1 DIQLTQSPSSLAVSAGENVMTSCKSSQSVLYSANHKNYLAWYQQKPGQSPKLLIYWASTR 60

Qy      61 ESGVPDRFTGSGSGTDFTLTISRQVEDLAIYYCHQYLSSWTFGGGTKLEIK 112
          |||
Db      61 ESGVPDRFTGSGSGTDFTLTISRQVEDLAIYYCHQYLSSWTFGGGTKLEIK 112

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<!--EndFragment-->

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<!--StartFragment-->RESULT 1

AAO27198

ID AAO27198 standard; protein; 123 AA.

XX

AC AAO27198;

XX

DT 17-SEP-2003 (first entry)

XX

DE Murine anti-CD22 antibody, RFB4, VH protein.

XX

KW Framework-patching; complementarity determining region; CDR; mouse;

KW murine; cytostatic activity; cancer; Non-Hodgkin's lymphoma;

KW gene therapy; rheumatoid arthritis; FR-patching; RFB4 VH; CD22; antibody.

XX

OS Mus sp.

XX

FH Key Location/Qualifiers

FT Domain 31. .35

FT /note= "Complementarity determining region (CDR) 1"

FT Domain 50. .66

FT /note= "Complementarity determining region (CDR) 2"

FT Domain 99. .112

FT /note= "Complementarity determining region (CDR) 3"

XX

PN WO2003002607-A1.

XX

PD 09-JAN-2003.

XX

PF 10-JUN-2002; 2002WO-US018512.

XX

PR 27-JUN-2001; 2001US-00892613.

XX

PA (LEUN/) LEUNG S S.

XX

PI Leung SS;

XX

DR WPI; 2003-210245/20.

XX

PT New re-engineered or framework-patched immunoglobulin, useful for

PT preparing a composition for treating cancer, preferably Non-Hodgkin's

PT lymphoma or rheumatoid arthritis.

XX

PS Example 1; Fig 1a; 66pp; English.

XX

CC The invention relates to a novel re-engineered or framework (FR)-patched  
 CC immunoglobulin, containing the heavy and/or light chain variable region  
 CC (VH/VL) sequences from a parent antibody. Within these chains, at least  
 CC one of the compartmentalised framework sequences, defined as FR1, FR2,  
 CC FR3 and FR4 are replaced, or patched, by the corresponding framework  
 CC sequences from the heavy and light chain immunoglobulin region of a  
 CC different species. The FR-patched immunoglobulin binds specifically to an  
 CC antigen with affinity comparable to, or within 3-fold of, that of the  
 CC parent immunoglobulin. The invention discloses the process of FR-patching  
 CC which is used to generate re-engineered immunoglobulin chains having one  
 CC or more complementarity determining regions (CDR's) from a donor  
 CC immunoglobulin and portions of framework sequences from one or more human  
 CC or primate immunoglobulins. The molecules obtained demonstrate cytostatic  
 CC activity as well as reduced or eliminated immunogenicity, whilst  
 CC maintaining the specificity and affinity of the parent antibody. The FR-  
 CC patched immunoglobulin is useful during the preparation of a composition  
 CC for treating cancer, preferably Non-Hodgkin's lymphoma and also during  
 CC the treatment of rheumatoid arthritis. Furthermore, the molecules of the  
 CC invention may also prove useful in gene therapy. The current sequence is  
 CC that of the murine anti-CD22 antibody, RFB4, VH protein of the invention

XX

SQ Sequence 123 AA;

Query Match 100.0%; Score 648; DB 1; Length 123;  
Best Local Similarity 100.0%;  
Matches 123; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTY 60  
|||||

Db 1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTY 60

Qy 61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAFWGQGT 120  
|||||

Db 61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAFWGQGT 120

Qy 121 VSA 123  
|||

Db 121 VSA 123

&lt;!--EndFragment--&gt;

<!--StartFragment-->RESULT 4

AAO27199

ID AAO27199 standard; protein; 107 AA.

XX

AC AAO27199;

XX

DT 17-SEP-2003 (first entry)

XX

DE Murine anti-CD22 antibody, RFB4, VL protein.

XX

KW Framework-patching; complementarity determining region; CDR; mouse;

KW murine; cytostatic activity; cancer; Non-Hodgkin's lymphoma;

KW gene therapy; rheumatoid arthritis; FR-patching; RFB4 VL; CD22; antibody.

XX

OS Mus sp.

XX

FH	Key	Location/Qualifiers
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FT	Domain	24. .34
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FT	/note= "Complementarity determining region (CDR) 1"	
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FT	Domain	50. .56
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FT	/note= "Complementarity determining region (CDR) 2"	
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FT	Domain	89. .97
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FT	/note= "Complementarity determining region (CDR) 3"	
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XX

PN WO2003002607-A1.

XX

PD 09-JAN-2003.

XX

PF 10-JUN-2002; 2002WO-US018512.

XX

PR 27-JUN-2001; 2001US-00892613.

XX

PA (LEUN/) LEUNG S S.

XX

PI Leung SS;

XX

DR WPI; 2003-210245/20.

XX

PT New re-engineered or framework-patched immunoglobulin, useful for

PT preparing a composition for treating cancer, preferably Non-Hodgkin's

PT lymphoma or rheumatoid arthritis.

XX

PS Example 1; Fig 1b; 66pp; English.

XX

CC The invention relates to a novel re-engineered or framework (FR)-patched  
 CC immunoglobulin, containing the heavy and/or light chain variable region  
 CC (VH/VL) sequences from a parent antibody. Within these chains, at least  
 CC one of the compartmentalised framework sequences, defined as FR1, FR2,  
 CC FR3 and FR4 are replaced, or patched, by the corresponding framework  
 CC sequences from the heavy and light chain immunoglobulin region of a  
 CC different species. The FR-patched immunoglobulin binds specifically to an  
 CC antigen with affinity comparable to, or within 3-fold of, that of the  
 CC parent immunoglobulin. The invention discloses the process of FR-patching  
 CC which is used to generate re-engineered immunoglobulin chains having one  
 CC or more complementarity determining regions (CDR's) from a donor  
 CC immunoglobulin and portions of framework sequences from one or more human  
 CC or primate immunoglobulins. The molecules obtained demonstrate cytostatic  
 CC activity as well as reduced or eliminated immunogenicity, whilst  
 CC maintaining the specificity and affinity of the parent antibody. The FR-  
 CC patched immunoglobulin is useful during the preparation of a composition  
 CC for treating cancer, preferably Non-Hodgkin's lymphoma and also during  
 CC the treatment of rheumatoid arthritis. Furthermore, the molecules of the  
 CC invention may also prove useful in gene therapy. The current sequence is  
 CC that of the murine anti-CD22 antibody, RFB4, VL protein of the invention

XX

SQ Sequence 107 AA;

Query Match 99.5%; Score 559; DB 1; Length 107;  
Best Local Similarity 99.1%;  
Matches 106; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 1 DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSILHSGVPS 60

Db 1 DIQMTQTSSLSASLGDRVTISCRASQDISNYLNWYQOKPDGTVKLLIYYTSILHSGVPS 60

Qy 61 KFSGSGSGTDYSLTISNLEQEDFATYFCQQGNTLPWTFGGGTKLEIK 107

[illegible]

Db 61 RFSGSGSGTDYSLTISNLEQEDFATYFCQQGNTLPWTFGGGTKLEIK 107

&lt;!--EndFragment--&gt;